



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)	
Salaun et al.)	Confirmation No. 8956
)	
Serial No.: 10/630,374)	Examiner: Gembeh, Shirley V
)	
Filed: July 30, 2003)	
)	
For: Novel Medicinal Product)	Art Unit: 1614
)	
)	

DECLARATION UNDER RULE 132

To Honorable Commissioner of Patents and Trademarks
Washington, D.C.

SIR:

I, Philippe Potin from the Centre national de la Recherche Scientifique, Station Biologique de Roscoff, Department of Marine Plants and Biomolecules Place Georges Teissier, 29680 ROSCOFF, France, declare

THAT I am graduated in Biology with a PhD degree from the University of Brest (Université de Bretagne Occidentale, UBO)

THAT I head the research team "Biochemistry of algal defenses" at the Roscoff Marine station

THAT I have carefully studied application N° 10/630,374.

THAT I am fully familiar with the technical domain of the invention disclosed in the said application and that I am co-

inventor in a patent application whose object is a method for preparing the metabolites 12-HETE and 11,12-EET.

THAT I have carefully studied the Office Action dated October 20, 2005 and the references therein relied upon as well as the amendment filed September 8, 2005 which is referred to in the action.

THAT my attention has been drawn in particular on the last sentence of the penultimate paragraph of page 4 of the action dated October 20, 2005, which paragraph refers to Herbertsson et al., the said last sentence stating

"... at page 242 right hand column, second paragraph states that TNF induced c-fos expression which appears to be dependent on formation of HETEs prevented differentiation to adipocytes".

THAT I have been requested to indicate whether the said passage of Herbertsson et al. renders obvious the use of 12-HETE in a method of inhibiting differentiation of a fibroblast to an adipocyte.

THAT my position is as follows.

THAT the passage in question does not identify 12-HETE.

THAT "HETEs" comprise at least three particular HETEs, among which 5-, 12- and 15-HETE.

THAT consequently in order to answer the above question it is necessary to carefully examine the references relied upon by Herbertsson, i.e. references 17-20 (line 18, right column, page 242).

THAT after a careful study, it appears that only one of the cited references (i.e. Haliday et al., 1995) appears to be relevant to comment the Herbertssons' assumptions. In this reference, it is shown that TNF rapidly induces the proto-oncogenes c-fos and c-jun in the adipogenic TA1 cell line and that these responses are differentially controlled by intracellular mediators derived from arachidonic acid. It is described that arachidonic acid, which is released in response to TNF, induces c-fos, but not c-jun mRNA in quiescent TA1 cells. Pretreatment of the cells with lipoxygenase inhibitors abolished the induction of c-fos by TNF, while the induction of c-jun was unaffected. In contrast, a cyclooxygenase inhibitor had no effect on either response. The reference by Haliday et al. also demonstrates that TNF stimulates production of lipoxygenase metabolites in TA1 cells and that one of these, 5-HPETE, induces c-fos, but not c-jun. These data suggest that TNF activates the c-fos pathway, via the release of arachidonic acid and its subsequent conversion to a 5-lipoxygenase metabolite.

THAT, by way of consequence, from Herbertsson, it may be deduced that 5-HETE may prevent preadipocyte differentiation by modulating c-fos expression but that nothing can be deduced for 12-HETE.

THAT it follows that Herbertsson does not render obvious the use of 12-HETE in the method claimed.

THAT my attention was also drawn to the last paragraph of pages 4 and 5 of the action.

THAT, with respect to the first of these two paragraphs, I underline that a correlation between c-fos expression in the TA1 cell line and the observed decrease in the amount of 12(S)-HETE in differentiated 3T3 cells does not permit to forecast the inhibiting activity of 12(S)HETE against differentiation of fibroblast to adipocytes.

THAT, with respect to the second of the said two paragraphs, one of ordinary skill in the art would not combine Yanni and Herbertsson, the property of HETES derivatives presented by Yanni as preventing some eye disorders (activation of mucin production) having not the slightest relation to the context of Herbertsson.

I, the undersigned, declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and, further, that these statements were made with the knowledge that wilful false statements and the like so made punishable by fine or imprisonment, or both, under Section 1001, of Title 18, of the United States Code, and that such wilful false statements may jeopardize the validity of the application or any patent issuing thereon.

A handwritten signature in black ink, appearing to read 'Potin', with a stylized flourish above it.

Date: January 18, 2006

Philippe Potin